Colourimetric Estimation of Cisapridge Using Iodine - Catechol Charge Tansfer Complex Formation

K.R. KRISHNAKUMAR*, R. RAJU
College of Pharmaceutical Sciences, Medical College, Trivandrum.

Received 15 April 1995

Cisapride is a substituted piperidinyl benzamide chemicaly related to metoclopramide. Its full chemical name is (±) cis-4-amino - 5 - chloro -N [1-[3-(4- flurophenoxy) propyl]] -3-methoxy-4-piperidinyl]-2-methoxybenzamide.[1]. The reported methods of analysis are the non-aqueous potentiometric method using Ag/AgC1 electrode[2] and the HPLC UV detection method, for the estimation from body fluids[3]. In the present communication the development of a colourimetric method based on charge transfer (CT) complex formation of cisapride with iodine and catechol is reported.

THE formation of CT complex involves transfer of electronic charge from an 'electron-rich' molecule (a Lewis - base donor) to an 'electron-deficient' molecule (a Lewis - acid acceptor)[4]. Aromatic amines belong to the class of CT donors. Hence, for cisapride, which has such an aromatic amino functional moiety, a CT complex method was tried to develop using iodine as CT acceptor[4]. Cisapride was precipitated with iodine in aqueous acid medium, filtered, dissolved in dehydrated alcohol, collected in acid phthalate buffer, mixed with 0.2% w/v catechol in water and developed the red coloured CT complex.

All the chemicals used were of Analar grade and used as such without further purification. The required quantity of cisapride monohydrate R.S. was weighed and dissolved in 6% v/v acetic acid to get a final concentration of 2 mg/ml. (484 g cisapride monohydrate R.S. is equivalent to 466 g of cisapride). Cisapride was extracted from the powder of five tablets, off twenty powdered tablets using 75.0ml methanol, filtered through Whatman no.1 filter paper, distilled out the methanol in a concealed system and collected the residue. Using this residue the sample solution of 2 mg/ml of cisapride can be prepared in 6% v/v acetic acid.

Iodine 0.02 N[5] and potassium hydrogen phthalate buffer solution pH 3.0[6] were prepared according to IP 1985 procedure. Acetic acid 6% v/v was prepared by dilution and catechol 0.2% w/v was prepared by weighing. All the reagents were prepared in distilled water.

All aliquot of cisapride (20-180 mcg/ml) was transferred into boiling tubes, made the volume of 6% v/v acetic acid equal in all the cases, pipetted 5.0 ml of 0.02 N iodine into all, mixed well and allowed to react for 30 minutes. Filtered out the precipitate formed using an ordinary filter paper and dissolved it using 12.0 ml of dehydrated alcohol. The alcohol extract was collected in 30.0 ml of phthalate buffer, mixed well, pipetted 1.5 ml of 0.2% w/v catechol into all flasks, mixed well, allowed to react for forty minutes, made upto the mark using water, mixed well and measured the absorbance versus reagent blank at λ max-490 nm using LKB-Biochrom spectrophotometer with 1 cm matched cells. (The mixing to be done only after complete collection of the alcoholic extract.)

***For Correspondence:**
Kuttickattil House,
Thrickalathoor P.O.,
Ernakulam (Dt) - 683 557 Kerala.

Analysis of cisapride tablets using proposed method and spectrophotometric method:

Sample	Declared amount	Amount found by UV spectrometric method.	Proposed method	Standard deviation	Percentage recovery
Tablet 1	10 mg.	10.20 mg	10.12 mg	0.106	100.16
Tablet 2	10 mg.	10.05 mg	9.995 mg	0.092	97.72

Beer's law obeyed in the concentration range of 20 to 180 mcg/ml. The tablet analysis was carried out as for the medium concentration of the calibration graph using single point standardisation method.

The red coloured complex has a maximum absorbance at 490 nm. Cisapride itself and all the reagents used were non-absorbing at this specific wavelength. The scanning was done using Shimadzu UV/visible (UV-2100) spectrophotometer. The CT complex was found to be stable for a period of 50 minutes. The maximum molar absorptivity was found to be $2.297 \times 10^3 1\ mol^{-1}\ cm^{-1}$. Interference of the excipient starch was observed during analysis. To overcome this extraction using methanol was developed. Through detailed study pH was optimised as 3.0, reaction temperature in the range of 25 to 35°C, precipitation time with iodine as 30 minutes and the reaction time with catechol as forty minutes. The results of reproducibility and recovery studies were also satisfactory.

We are thankful to M/s. Systopic Laboratories Pvt.Ltd., for providing pure sample of cisapride. We also thank Dr. C.S.P. Iyer, Dr. S.V.Ramakrishna and Dr. Emilia Abraham of the RRL Trivandrum for the help extended during various stages of the work.

REFERENCES :

1. CIMS Drug profiles, Vol.2, No.2, June 1993, 5.
2. Janssen Research Foundation, Analytical Research, PC-RS 90-1 (900222) -R 51619 - Polymorph II, 5
3. R.Woestenborghs, W.Lorreyne, F.Van Rompey and J.Heykants, **J. Chromatogr, Biomed. Appl.**, 1988, 424, 195.
4. William Kemp, Organic Spectroscopy, 3rd edn., 1991, ELBS, 274.
5. Pharmacopoeia of India, 3rd edn., 1985, Vol.II, A-245.
6. Pharmacopoeia of India, 3rd edn., 1985, Vol.II, A-142.